Remarks

The Office Action mailed July 25, 2003 has been received and reviewed. Claims 39-53 having been canceled and claims 54-77 having been added, the pending claims are claims 54-77.

New claims 54, 57, 60-63, and 66-74 are supported, for example, by claims 39, 40, 41-44, and 45-53 (now canceled), respectively. New claim 58 is supported, for example, by claims 39 and 44 (now canceled). New claim 75 is supported, for example, by claims 44 and 50 (now canceled). New claims 55-56, 59, 64-65, and 76-77 are generally supported by the specification (e.g., page 24, line 8 to page 31, line 28). Applicants respectfully submit that it is well known to one of skill in the art that *Porphyromonas gingivalis* is a gram-negative bacteria (e.g., claims 55 and 64). Claims 54, 60, 63, 71, and 75 recite the proviso that "the second amino acid from the unblocked amino-terminal end of the polypeptide is not charged," which is supported by the specification at, for example, page 29, lines 21-22 (i.e., "charged amino acids not being acceptable as the second amino acid from the N-terminal end of the polypeptide") and page 30, lines 1-2 (i.e., "did not cleave model substrates with blocked amino-termini").

Claims 54-77 have been added to more concisely define the present invention in the format similar to that exemplified in the "Revised Interim Written Description Guidelines Training Materials" (hereinafter "Guidelines") issued by the United States Patent and Trademark Office. Notably, in one example, the Guidelines state that although only a single species was disclosed, the claimed genus meets the written description requirement through recitation of "hybridization conditions in combination with . . . function." Further, in another example, the Guidelines state that although only a single species was disclosed, the claimed genus meets the written description requirement through recitation of function and structural identity in the claim, and the disclosure of "an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity."

Finally, Applicants also note that none of the presently pending claims recites the language "active analog, active fragment, or active modification."

Reconsideration and withdrawal of the rejections are respectfully requested.

Examiner's Interview

Applicants thank the Examiner for granting Applicants' Representative, Loren D. Albin, a telephonic interview with the Examiner on October 21, 2003.

Applicants' Representative requested clarification of the status of the Office Action mailed July 25, 2003, because while the "Final" box on the Office Action Summary sheet was checked, the body of the Office Action was silent regarding finality. The Examiner confirmed that the Office Action mailed July 25, 2003 is non-final.

The rejection of claims 39 and 41-53 under 35 U.S.C. §112, second paragraph, as being indefinite for reciting "aliphatic or aromatic residue" was discussed. Applicants' Representative requested clarification of the Examiner's remarks concerning whether tyrosine is polar or aromatic, since aromatic is clearly defined in the specification, and the question of whether residues are aromatic or polar are not relevant to the pending claims. No agreement was reached, but the Examiner agreed to call Applicants' Representative after discussing the issue with her Supervisor. The Examiner called Applicants' Representative, Loren D. Albin, on October 23, 2003, and agreed that the above discussed rejection would be dropped if Applicants listed on the record the amino acids that are intended to be included in the above definition. Applicants Representative noted that providing an exhaustive list of such amino acids is not possible (e.g., due to unusual and/or modified amino acids), but did agree to provide an exemplary list of common amino acids that are intended to be included in the above definition.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 39 and 41-53 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleged that the term "aliphatic or aromatic residue" is indefinite, as specific amino acids are not recited. Claims 39 and 41-53 having been canceled, the rejection is rendered moot. However, to the extent that the rejection applies to new claims 54-77, Applicants respectfully traverse the rejection.

The present claims define dipeptidylpeptidase amidolytic activity as "activity for cleaving the peptide bond between the second and the third amino acids from the unblocked amino-terminal end of a target polypeptide having an aliphatic or an aromatic residue as a substituent on the α-carbon atom of the second amino acid from the unblocked amino-terminal end of the polypeptide, with the proviso that the second amino acid from the unblocked amino-terminal end of the polypeptide is not charged." The specification clearly states that "aliphatic residue" means an organic radical having carbon atoms linked in open chains, and that "aromatic residue" means an organic radical that includes an aromatic ring (e.g., an aromatic group, an alkaryl group, or an aralkyl group) (e.g., page 6, lines 26-29). Charged amino acids, e.g., arginine, lysine, histidine, aspartic acid, and glutamic acid, as clearly recited in the specification (e.g. page 14, lines 4-7) are excluded by the "proviso" language. Amino acids having no substituents on the α-carbon atom (e.g., glycine) are also excluded by the above definition. Proline, a cyclic residue that has neither an aromatic residue or an aliphatic (i.e., open chain) residue as a substituent on the α-carbon atom, is also excluded by the above definition. Thus, Applicants respectfully submit that it would be clear to one of skill in the art, based on reading the specification as a whole, that common, non-charged amino acids having an aliphatic or an aromatic residue as a substituent on the α-carbon atom include, for example, alanine, asparagine, cysteine, 3,5-dibromotyrosine, 3,5-diiodotyrosine, glutamine, isoleucine, leucine, methionine, phenylalanine, serine, threonine, thyroxine, tryptophan, tyrosine, and valine.

The Examiner rejected claims 39 and 41-53, alleging that the recitation of "modification" rendered the claims indefinite. Claims 39 and 41-53 having been canceled, the rejection is rendered moot. Applicants also note that none of new claims 54-77 recite the term "modification."

The Examiner also rejected claims 44-49, alleging that the recitation of "catalytic domain" renders the claims indefinite. Claims 44-49 having been canceled, the rejection is rendered moot. Applicants respectfully note that none of new claims 54-77 recite "catalytic domain."

Rejection under 35 U.S.C. §112, First Paragraph

Lack of Enablement

The Examiner rejected claims 39 and 41-50 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner noted that the specification is enabling for the dipeptidylpeptidase encoded by SEQ ID NO:1, but alleged that the specification does not provide enablement commensurate in scope with the invention as claimed. Claims 39 and 41-50 have been canceled, but to the extent that the rejection is maintained and applies to new claims 54, 60-63, and 66-71, Applicants respectfully traverse the rejection.

"A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." M.P.E.P. §2164.04. "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." M.P.E.P. §2164.01(b). "For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be *used* in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not *use* the genus as a whole without undue experimentation." M.P.E.P. §2164.02, paragraph entitled "WORKING EXAMPLES AND A CLAIMED GENUS" (emphasis added). "[E]ven in unpredictable arts, a disclosure of every operable species is not required." M.P.E.P. §2164.03.

The specification clearly describes methods of making the claimed isolated nucleic acids (e.g. page 9, line 22 to page 12, line 26; and page 15, line 2 to page 20, line 25). Although not required, and as admitted by the Examiner, Applicants have even provided working examples of the claimed isolated nucleic acids (e.g. pages 24-27). Further, the specification provides methods of using the claimed isolated nucleic acids (e.g., page 20, line 26 to page 23, line 20). Notably, the Examiner has not provided any reason to doubt the objective truth of the disclosure provided in the specification.

In spite of the disclosure provided in the specification as noted above, the Examiner asserted that "the specification does not reasonably provide enablement for "any nucleic acid molecule encoding any dipeptidylpeptidase amidolytic activity" (page 5, first full paragraph, of the Office Action mailed July 25, 2003). Applicants are not claiming "any nucleic acid molecule encoding any dipeptidylpeptidase amidolytic activity."

Independent claims 54, 60, 63, and 71 claim isolated nucleic acids by reciting physical and/or chemical properties including, for example, hybridization conditions (e.g., independent claim 54), specific sequences (e.g., independent claim 60), and/or structural identity (e.g. independent claims 63 and 71), as further described herein below under the remarks to the rejection based on lack of written description. Independent claims 54, 60, 63, and 71 claim isolated nucleic acids by further reciting function (e.g., encoding a "protein [and variants thereof having] dipeptidylpeptidase amidolytic activity").

Further, Applicants respectfully reiterate that, as quoted from the M.P.E.P. herein above, *a disclosure of every operable species is not required.* Applicants respectfully submit that one of skill in the art, using the disclosure provided in the specification (including the working examples), would be able to make and use the entire scope of the invention as recited in, for example, independent claims 54, 60, 63, and 71. For example, the specification provides guidance to one of skill in the art in selecting amino acids for substitution into the encoded peptidase (e.g., page 13, line 31 to page 14, line 10). Further, Applicants respectfully submit that one of skill in the art, in view of the present specification, would be enabled to select appropriate

amino acids in the peptidase as candidates for substitution (e.g., page 14, line 11 to page 15, line 2).

Moreover, the specification provides one of skill in the art exemplary methods of assaying isolated nucleic acids for amidolytic activity (e.g., page 12, line 27 to page 13, line 25; page 25, line 22 to page 26, line 2; and page 26, lines 23-32).

Applicants respectfully request that the rejections under 35 U.S.C. §112, first paragraph, for lack of enablement, be reconsidered and withdrawn.

Lack of Written Description

The Examiner rejected claims 39 and 41-50 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the Office Action mailed July 25, 2003, the Examiner admitted that the present specification provides adequate written description for claims 40 and 51-53, but not for a genus of nucleic acids as recited in claims 39 and 41-50. Claims 39 and 41-50 have been canceled, but to the extent that the rejection is maintained and applies to new claims 54, 60-63, and 66-71, Applicants respectfully traverse the rejection.

"The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice . . ., reduction to drawings . . ., or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. . . . [T]here may be situations where one species adequately supports a genus." M.P.E.P. §2163(II)(A)(3)(a)(ii).

Without more, the disclosure of one species (e.g., SEQ ID NO:1 or SEQ ID NO:2), arguably may not support a genus of nucleic acids or proteins. However, the present claims

provide more than the bare sequence of one nucleic acid or one protein. Applicants respectfully submit that the present claims satisfy the written description requirement of 35 U.S.C. §112, first paragraph, for at least the reasons discussed herein below.

CLAIM 54 RECITES HYBRIDIZATION CONDITIONS IN COMBINATION WITH FUNCTION

Claim 54 recites an isolated nucleic acid, the complement of which hybridizes to SEQ ID NO:1 (i.e., hybridization conditions). Claim 54 further recites that the isolated nucleic acid encodes a protein having dipeptidylpeptidase amidolytic activity (i.e., function). Thus, claim 54 defines a genus through recitation of hybridization conditions in combination with function. As discussed herein above, Applicants note that the Guidelines state that although only a single species is disclosed, the claimed genus meets the written description requirement through recitation of hybridization conditions in combination with function.

Thus, Applicants respectfully submit that claim 54 and dependent claims 55-59 satisfy the written description requirement under 35 U.S.C. §112, first paragraph. In addition, Applicants note that dependent claim 58 further recites structural identity as described herein below.

CLAIMS 58, 63, AND 66-75 RECITE BOTH FUNCTION AND STRUCTURAL IDENTITY, AND THE SPECIFICATION PROVIDES AN ASSAY FOR IDENTIFYING PROTEINS WITH DIPEPTIDYLPEPTIDASE AMIDOLYTIC ACTIVITY

Claims 58, 63, and 66-75 recite a protein [and variants therof] having diipeptidylpeptidase amidolytic activity (i.e., function).

Claims 58, 63, 66-70, and 75 further recite a protein [and variants thereof] having a percentage amino acid identity of greater than 40% (e.g., claims 58, 63, and 75), 50% (e.g., claim 66), 60% (e.g., claim 67), 70% (e.g., claim 68), 80% (e.g., claim 69), or 90% (e.g., claim 70), with SEQ ID NO:2 (i.e., structural identity). Claims 71-75 further recite an isolated nucleic acid comprising a nucleotide sequence having at least about 70% identity (e.g., claims 71 and 75), 80% identity (e.g., claim 72), 90% identity (e.g., claim 73), or 95% identity (e.g., claim 74),

with SEQ ID NO:1 (i.e., structural identity). Notably, as described herein above, claim 75 recites structural identity to both a protein and a nucleotide sequence.

The specification describes an assay for identifying proteins having dipeptidylpeptidase amidolytic activity (e.g., page 12, line 27 to page 13, line 25; page 25, line 22 to page 26, line 2; and page 26, lines 23-32).

Thus, claims 58, 63, and 66-75 define a genus through the recitation of both function and structural identity, and the specification provides an assay for identifying dipeptidylpeptidase amidolytic activity. As discussed herein above, Applicants note that the Guidelines state that although only a single species is disclosed, the claimed genus meets the written description requirement through recitation of function and structural identity in the claim, and the disclosure of an assay for identifying variants which are capable of the specified catalytic activity.

Thus, Applicants respectfully submit that claims 58, 63, and 66-75 and dependent claims 64-65 and 76-77 satisfy the written description requirement under 35 U.S.C. §112, first paragraph.

CLAIMS 60-62 RECITE BOTH FUNCTION AND A SPECIFIC SEQUENCE, AND THE SPECIFICATION PROVIDES AN ASSAY FOR IDENTIFYING PROTEINS WITH DIPEPTIDYLPEPTIDASE AMIDOLYTIC ACTIVITY

Claims 60-62 each recite a protein having dipeptidylpeptidase amidolytic activity (i.e., function).

Claims 60-62 each recite that the protein has a sequence comprising the residues 543 to 712 (e.g., claim 60), 540 to 712 (e.g., claim 61), or 522 to 712 (e.g., claim 62) of SEQ ID NO:2. Thus, claims 60-62 each recite a protein that includes a specific amino acid sequence having 170, 173, or 191 amino acid residues, respectively. Significantly, the specific sequences include the active site and regions of homology observed when aligning the putative homologues (e.g., Figure 6 of the present application).

Further, the specification describes an assay for identifying proteins having dipeptidylpeptidase amidolytic activity (e.g., page 12, line 27 to page 13, line 25; page 25, line 22 to page 26, line 2; and page 26, lines 23-32).

Thus, Applicants respectfully submit that one of skill in the art would recognize that Applicants were in possession of the genus of proteins that include the recited function and sequence.

In view of the amendments and remarks presented herein, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §112, first paragraph, for lack of written description. In the event that rejections are not withdrawn, Applicants respectfully request that the Examiner specifically point out any missing support that is suggested by the "Revised Interim Written Description Guidelines Training Materials" issued by the United States Patent and Trademark Office, as Applicants have made an earnest attempt to provide claims that satisfy the written description requirement under 35 U.S.C. §112, first paragraph, along with remarks to describe how the requirement is specifically satisfied by each claim.

Rejection under 35 U.S.C. §102

P. Gingivalis genomic contig gln/TIGR/P. gingivalis_1208

The Examiner rejected claims 39-53 under 35 U.S.C. §102(a) or (b) as being anticipated over the sequence designated "P. Gingivalis genomic contig gln/TIGR/P. gingivalis_1208," which the Examiner alleged is admitted prior art by Applicants. Claims 39-53 having been canceled, the rejection is rendered moot. However, to the extent the rejection applies to new claims 54-77, Applicants respectfully traverse the rejection.

For anticipation to occur, a prior art disclosure must put the public in possession of the invention. *See, for example*, M.P.E.P. §2121.01. Applicants respectfully submit that the sequence designated "P. Gingivalis genomic contig gln/TIGR/P. gingivalis_1208" does not contain an enabling disclosure, and thus, did not put the public in possession of the claimed invention.

Independent claims 54, 60, 63, 71, and 75 each recite "[a]n isolated nucleic acid." The specification recites that "the term 'isolated' means that a polypeptide or a polynucleotide has been either removed from its natural environment, produced using recombinant techniques, or chemically or enzymatically synthesized" (specification at page 6, lines 8-10).

In contrast, the TIGR database disclosed contigs that are part of the *P. gingivalis* genome in the Unfinished Microbial Genomes database, and Applicants are not claiming such contigs or the unfinished genome. Moreover, the sequence designated "P. Gingivalis genomic contig gln/TIGR/P. gingivalis_1208" provides no guidance as to which sequence of nucleotides might or might not contain an open reading frame. Further, there is no disclosure as to which nucleotide sequence, if any, might encode a protein. Thus, a person of ordinary skill, having the nucleotide sequence of the genomic clone, would not be able to predict that the open reading frame encoding SEQ ID NO:1 could be transcribed or translated. Applicants respectfully submit that the disclosure of the unfinished genome is not an enabling disclosure for making the presently claimed isolated nucleic acids (e.g., independent claims 54, 60, 63, 71, and 75), and thus, fails to anticipate claims 54-77.

Nonetheless, the Examiner referred to www.pgingivalis.org/ (2002) (Duncan et al.) as support for isolated genomic DNA polynucleotides, and alleged that "[o]ne or more relevant isolated DNA molecules used for sequencing, including contig gln/TIGR/p. gingivalis_1208, *inherently* comprise the polynucleotide of SEQ ID NO:1" (page 13 of the Office Action mailed July 25, 2003; emphasis added). Applicants respectfully traverse the Examiner's allegation.

According to M.P.E.P. §2112 "[t]o establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the document, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. . . . In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." M.P.E.P §2112 (emphasis in original).

First, Duncan et al., in describing their "shotgun" approach to sequencing state that "[a] random library is best constructed from mechanically sheared fragments since any kind of enzymatic cleavage is generally non-random. [S]heared DNA fragments are blunt-ended, gel fractionated and inserts of average size 1.8-2.5 kb are cloned into pUC18" (Duncan et al., page 3, entitled "Constructing random genomic libraries of *P. gingivalis* DNA," second paragraph). Applicants respectfully submit that none of the random 1.8-2.5 kb mechanically sheared DNA fragments disclosed by Duncan et al. *necessarily* include the entire 2139 nucleotide (2139 kb) sequence, SEQ ID NO:1. Thus, it is respectfully submitted that the Examiner has not met her burden of providing a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the cited document.

Moreover, even if one of the random mechanically sheared DNA fragments disclosed by Duncan et al. *arguably* did include the entire 2139 nucleotide sequence, SEQ ID NO:1, there is no teaching or suggestion in Duncan et al. to provide guidance as to which random mechanically sheared DNA fragment might or might not contain an open reading frame. Further, there is no disclosure as to which random mechanically sheared DNA fragment, if any, might encode a protein. Thus, a person of ordinary skill, having the random mechanically sheared DNA fragments, would not be able to predict that the open reading frame encoding SEQ ID NO:1 could be transcribed or translated.

Second, the Examiner is apparently attempting to equate a "contig" (i.e., gln/TIGR/p. gingivalis_1208) disclosed on the Unfinished Microbial Genomes database, TIGR, with one of the random mechanically sheared DNA fragments disclosed by Duncan et al. Applicants respectfully note that Duncan et al. clearly describe that the assembly of clones results in contigs:

> Assembly of the genome sequence will be performed using TIGR Assembler (Sutton et al., 1995) which simultaneously clusters and assembles fragments of the genome using a best-match-first strategy. Potentially chimeric fragments and fragments representing the boundaries of repetitive regions are flagged based on

> partial mismatches at the ends of alignments and excluded from the contig. TIGR Assembler recognizes potentially repetitive regions (those present at more than one copy in the genome) based on 10-mer oligonucleotide frequency. Contig building in repetitive regions is more stringent than in non-repetitive regions to attempt to distinguish among closely related copies of the repeat element. (Duncan et al., page 4, under the heading "Assembly")

Thus, Applicants respectfully submit that contigs are not necessarily the same as the random mechanically sheared DNA fragments disclosed by Duncan et al.

Nonetheless, the Examiner alleged that "specific polynucleotide sequences encoding dipeptidylpeptidase and amidolytic activities can be easily identified by analyzing the sequence of the P. Gingivalis TIGR database using commercially available programs such as ProSite" (page 13 of the Office Action mailed July 25, 2003). To the extent that the Examiner is basing the present 35 U.S.C. §102 rejection on an "obvious to try" rationale, Applicants respectfully submit that such a rationale is not appropriate for either an anticipation rejection under 35 U.S.C. §102 or an obviousness rejection under 35 U.S.C. §103. *See, for example*, M.P.E.P. §§2121.01 and 2143.01.

Thus, Applicants respectfully submit that the Examiner has failed to present a *prima facie* case for the unpatentability of present claims 54-77 over the sequence designated "P. Gingivalis genomic contig gln/TIGR/P. gingivalis_1208," which the Examiner alleged is admitted prior art by Applicants.

U.S. Pat. No. 6,444,799 (Ross et al.)

The Examiner rejected claims 39 and 41-53 under 35 U.S.C. §102(e) as being anticipated by U.S. Pat. No. 6,444,799 (Ross et al.). Applicants respectfully traverse the rejection. Claims 39-53 having been canceled, the rejection is rendered moot. However, to the extent the rejection applies to new claims 54-77, Applicants respectfully traverse the rejection.

Ross et al., in describing their "shotgun" approach to sequencing, state that "purified genomic DNA from *P. gingivalis* was nebulized to fragment the DNA and was treated with Bal31 nuclease to create blunt ends then run twice through preparative 1% agarose gels. DNA

fragments of 1.6-2.0 kb were excised from the gel and the DNA recovered" (column 6, lines 44-49). Ross et al. disclose the sequences of 1,120 different DNA fragments (i.e., SEQ ID NOs:1-1120). However, Ross et al. lack a disclosure that any of the 1,120 different DNA fragments encode any protein. Ross et al. also lack a disclosure or suggestion of a protein having dipeptidylpeptidase amidolytic activity.

Moreover, there is no teaching or suggestion in Ross et al. to provide guidance as to which DNA fragments might or might not contain an open reading frame. Further, there is no disclosure as to which DNA fragment, if any, might encode a protein. Thus, a person of ordinary skill, having the 1,120 DNA fragments disclosed by Ross et al., would not be able to predict that the open reading frame encoding SEQ ID NO:1 could be transcribed or translated.

Nonetheless, the Examiner pointed to SEQ ID NO:726 disclosed by Ross et al. The only guidance provided by Ross et al. in selecting any specific DNA fragments (i.e, SEQ ID NOs) from the 1,120 disclosed DNA fragments, is in claims 1 and 4-6, each of which recites SEQ ID NOs: 176, 192, 214, 243, 273, 417, 524, 638, 758 and 1005. Thus, nothing in Ross et al. would provide guidance for one of skill in the art to select SEQ ID NO:726 from the 1,120 DNA fragments disclosed by Ross et al. In fact, by pointing specifically to SEQ. ID. NOS: 176, 192, 214, 243, 273, 417, 524, 638, 758 and 1005 in the claims, Applicants respectfully submit that Ross et al. actually teach away from selecting SEQ ID NO:726. Moreover, Ross provides no disclosure or suggestion that any of the 1,120 disclosed DNA fragments might encode a protein having the presently claimed dipeptidylpeptidase amidolytic activity.

Nonetheless, the Examiner asserted that SEQ ID NO:726 disclosed by Ross et al. "encodes a polypeptide" and refers to "the polypeptide of Ross et al" and "the protein of Ross et al" (page 14 of the Office Action mailed July 25, 2003). Applicants reiterate that Ross et al. fail to disclose any polypeptides or proteins, and additionally lack a disclosure that any of the 1,120 different DNA fragments disclosed encode any protein.

Further, the Examiner alleged that "*the polypeptide of Ross et al* has some homology with *known proteases*, including a protease comprising the serine protease motif of SEQ ID NO:25" (page 14 of the Office Action mailed July 25, 2003; emphasis add d). As the *known protease*,

the Examiner is apparently referring to sequence accession number gi:9968803 listed on the BLAST search provided by the Examiner as document "X" on the PTO-892 form. Applicants note that the complete listing for sequence accession number gi:9968803 on NCBI (EXHIBIT A) describes the sequence as a "glutamyl endopeptidase." The present specification recites that "the *P. gingivalis* DPP-7 displays the consensus sequence characteristic for the catalytic site of the V-8 like proteases, a group of *endopeptidases cleaving after glutamic or aspartic acid residues*" (page 11, lines 18-20; emphasis added). Notably, proteins having dipeptidylpeptidase amidolytic activity, as defined in the present claims, do not cleave the peptide bond between the second and the third amino acids from the N-terminal end of a target polypeptide when the second amino acid from the N-terminal end of the polypeptide is a glutamic or aspartic acid residue (i.e., a charged residue; *see, for example,* the specification at page 14, lines 4-7). Moreover, the specification recites that "[t]he protease did not show any *endopeptidase activity* on gelatin, insulin ß chain, carboxymethylated lysosyme, azocazein or type I collagen" (page 29, lines 23-24; emphasis added). Based on the remarks presented herein above, Applicants respectfully submit that one of skill in the art would not "reasonably believe that the protein of Ross et al inherently has dipeptidylpeptidase amidolytic activity," as alleged by the Examiner (page 14 of the Office Action mailed July 25, 2003).

Moreover, SEQ ID NO:726 disclosed by Ross et al. is a sequence of 1974 base pairs. Thus, SEQ ID NO:726 is not identical to a sequence recited in certain preferred embodiments of the presently claimed invention, e.g., the 2139 nucleotide sequence, SEQ ID NO:1 (e.g., claims 57 and 76), nor can it encode a protein recited in certain preferred embodiments of the presently claimed invention, e.g., the 712 residue protein, SEQ ID NO:2 (e.g., claims 59 and 77).

Further, the local alignment provided by the Examiner indicated that the protein allegedly encoded by SEQ ID NO:726 disclosed by Ross et al. did not include a segment that would be identical to segments recited in certain preferred embodiments of the presently claimed invention, e.g., residues 543 to 712 of SEQ ID NO:2 (e.g., claim 60); residues 540 to 712 of SEQ ID NO:2 (e.g., claim 61); or residues 522 to 712 of SEQ ID NO:2 (e.g., claim 62).

In addition, the local alignment provided by the Examiner indicated that SEQ ID NO:726 disclosed by Ross et al. shared 1730 identical nucleotides with the 2139 nucleotide sequence, SEQ ID NO:1, resulting in 81% identity with SEQ ID NO:1 (100 x 1730/2139), which is less than the identities recited in certain preferred embodiments of the present invention, e.g., at least about 90% identity (e.g., claim 73) and at least about 95% identity (e.g., claim 74). Similarly, the local alignment provided by the Examiner indicated that the protein allegedly encoded by SEQ ID NO:726 disclosed by Ross et al. shared 576 identical residues with the 712 residue sequence, SEQ ID NO:2, resulting in 81% identity with SEQ ID NO:2 (100 x 576/712), which is less than the identities recited in certain preferred embodiments of the present invention, e.g., greater than 90% (e.g., claim 70).

Thus, Applicants respectfully submit that the Examiner has failed to present a *prima facie* case of unpatentability of present claims 54-77 over Ross et al.

Based on the remarks presented herein above, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §102.

PTO-1449 Form

Applicants are submitting herewith a PTO-1449 form listing and including copies of underlying documents for sequence accession number gi:9968803 listed on the BLAST search provided by the Examiner as document "X" on the PTO-892 form, as described herein above. The underlying documents include the complete listing for sequence accession number gi:9968803 on NCBI (EXHIBIT A), and the document cited with the sequence accession number, Yokoi et al., *Gene*, 281:115-122 (December 2001). As the sequence accession number has been made of record by the Examiner, Applicants respectfully submit that no fee is due. However, in the event that the Examiner disagrees and a fee is due, please charge any fee or credit any overpayment to Account No. 13-4895. Consideration of each of the documents listed on the attached 1449 form is respectfully requested. Pursuant to the provisions of M.P.E.P. §609, Applicants further request that a copy of the 1449 form, marked as being considered and initialed by the Examiner, be returned with the next Official Communication.

Summary

It is respectfully submitted that all the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
James TRAVIS et al.

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October 27, 2003
Date

By: _____
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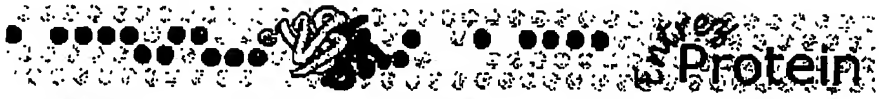
CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 27 day of October, 2003, at 4:21 p.m. (Central Time).

By: _____
Name: Rachel Caglindi-Graben



☐ 1: CAC06168. glutamyl endopept...[gi:9968803]

BLink, Domains, Links

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LOCUS       CAC06168                316 aa            linear   BCT 05-OCT-2002
DEFINITION  glutamyl endopeptidase [Staphylococcus warneri].
ACCESSION   CAC06168
VERSION     CAC06168.1  GI:9968803
DBSOURCE    embl locus SWA293885, accession AJ293885.2
KEYWORDS    .
SOURCE      Staphylococcus warneri
  ORGANISM  Staphylococcus warneri
            Bacteria; Firmicutes; Bacillales; Staphylococcus.
REFERENCE   1
  AUTHORS   Yokoi,K., Kakikawa,M., Kimoto,H., Watanabe,K., Yasukawa,H.,
            Yamakawa,A., Taketo,A. and Kodaira,K.I.
  TITLE     Genetic and biochemical characterization of glutamyl endopeptidase
            of Staphylococcus warneri M
  JOURNAL   Gene 281 (1-2), 115-122 (2001)
  MEDLINE   21623048
   PUBMED   11750133
REFERENCE   2
  AUTHORS   Kakikawa,M.
  TITLE     Direct Submission
  JOURNAL   Submitted (30-AUG-2000) Kakikawa M., Molecular Biology Group,
            Toyama University, 3190 Gofuku, Toyama, 930-8555, JAPAN
  REMARK    revised by author [08-AUG-2002]
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Exhibit A